

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Application of ARENA, Jose F.

Confirmation No: 8505

Application No.: 10/687,328

Examiner: SWITZER, Juliet Caroline

Date Filed: October 16, 2003

Group: 1634

For: BRCA1/BRCA2 SCREENING PANEL

Mail Stop Amendment
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

37 C.F.R § 1.132 DECLARATION

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Lisa Baumbach-Reardon, PhD, declare as follows:

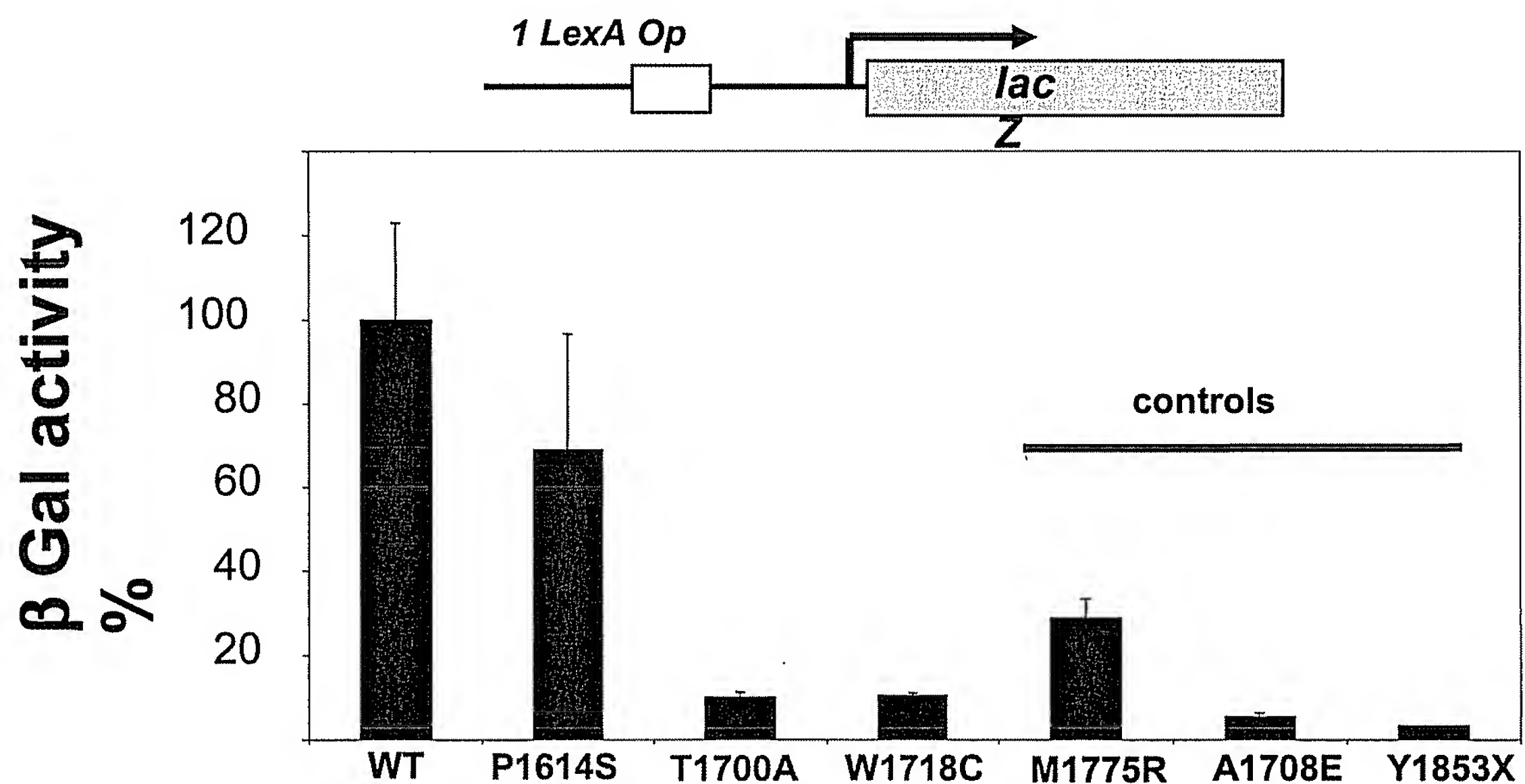
1. I am a co-inventor of the patent application No. 10/687,328 entitled "BRCA1/BRCA2 SCREENING PANEL " (hereafter the '328 application) and the subject matter described therein.
2. I hold a PhD degree in Biochemistry and Molecular Biology and currently am working in Biomedical Science. I am presently an Associate Research Professor at the University of Miami, Miami, Florida.

3. Following submission of the patent application No. 10/687,328 on October 16, 2003, I have continued working on the invention as shown below as **Exhibit A**. **Exhibit A-1** contains a graph showing results from experimental assays, which determines possible functional effects of *BRCA1* missense variants using a transcriptional assay for mutations in the *BRCA1 BRCT* domains. As is shown in this graph, wild-type (WT) normal control gives 100% activity, whereas *BRCA1* missense mutation T1700A gives only approximately 10% activity, clearly demonstrating its deleterious effect on *BRCA1 BRCT* activity, hence increasing risk for breast cancer. Also illustrated are assay results for several other *BRCA1* mutations.
4. **Exhibit A-2** contains a table summarizing information on three novel *BRCA1* missense mutations (W1718C; T1700A; P1614S) identified in my laboratory in three unrelated African-American breast cancer patients. Three independent experiments were performed – Segregation Analysis (tracking mutation through the family); Prevalence in 50 control (unaffected) African-American women; and functional assay explained above (**Exhibit A-1**). In reference to mutation T1700A, we were unable to perform the segregation analysis (not enough family members available; N/A), however, the mutation was not present in the control samples analyzed, and clearly demonstrated a deleterious effect on *BRCA1 BRCT* activity (**Exhibit A-1**).

5. These experimental results show that there is an association between the nucleotide present at position 5217 (mutation T1700A) in the *BRCA1* gene and the risk of breast cancer development in African American women.
6. Exhibit A

Exhibit A-1

Functional analysis of *BRCA1* missense variants using a transcriptional assay for mutations in the *BRCA1* BRCT domains.



37 C.F.R. §1. 132 DECLARATION
In re Application of: ARENA et al.
Confirmation No: 8505
Application No.: 10/687,328
Page - 4 -

Exhibit A-2

<u>BRCA1 Variant</u>	<u>Segregation Analysis</u>	<u>Control Prevalence</u>	<u>Functional Assay</u>
W1718C	++	0	Deleterious
T1700A	N/A	0	Deleterious
P1614S	N/A	0	Partial deleterious

Summary

Experimental data reported here provide further evidence to demonstrate that the presence of an adenine to guanine transition at position 5217 (mutation T1700A) in the *BRCA1* gene is associated with breast cancer in African American women.

5. I state that all experimental data provide herein are true. I further state that all statements made herein are true and that all statements made on information and experimental results under their experimental conditions are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 6/11/07

Lisa Baumbach-Reardon, Ph.D.
Lisa Baumbach-Reardon, Ph.D.